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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/549,596

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YADID1

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EXAMINER

CROUCH, DEBORAH

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/549,596	<b>Applicant(s)</b> YADID ET AL.	
	<b>Examiner</b> Deborah Crouch	<b>Art Unit</b> 1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 22 October 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-3 and 6-32 is/are pending in the application.  
4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) 16-27 is/are allowed.
- 6) ☒ Claim(s) 1-3, 6-8, 10-13, 15 and 28 is/are rejected.
- 7) ☐ Claim(s) 9, 14 and 29-32 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 19 September 2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☒ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

Applicant's arguments filed October 22, 2008 have been fully considered but they are not persuasive. The amendment has been entered. Claims 1-3 and 6-32 are pending.

### ***Claims***

Claims 16-27 and 29-32 are allowable. Claims 9, 14 and 29-32 would be allowable if written in independent form.

### ***Art Rejections and Response to Arguments***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-3, 6, 7, 10, 12, 13 and 28 remain rejected under 35 U.S.C. 102(b) as being clearly anticipated by Diamond et al. (1999) Hippocampus, Vol. 9, pp. 542-552 for reasons set forth in the office action mailed April 22, 2008.

Diamond teaches rats conditioned to exhibit recurrence of trauma upon repeated exposures to a cat (page 547, figure 1). As is evident from the data presented in figure 1, rats exposed to a cat several days in a row, showed decreasing memory retention in the six-arm maze test, with a confidence of  $P < .05$  (page 547, figure 1, legend, lines 1-

6). As there are no structural differences between the animals claimed and those of Diamond, the particular phenotypes claimed, Wolframin and Sigma 1 receptor levels or having 2 or 3 PTSD behaviors would be inherent to the rats of Diamond.

The animals are claimed to exhibit PTSD-like behavior consisting of re-experiencing a trauma in response to a stimulus, avoidance of social interaction, and hyper-arousal in response to a stimulus. The rats of Diamond re-experienced trauma associated with repeated exposure to a cat as evidenced by decreased memory retention. Further, the decreasing memory retention in the water maze test can be considered evidence of a hyper-arousal response to a stimulus not associated with the trauma. The specification does define "hyper arousal" to eliminate the water maze test. Diamond also states rats exposed to a cat exhibited an increase in corticosterone levels (Diamond, page 543, col. 1, parag. 3, lines 10-13).

Claim 15 is rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Diamond et al. (1999) Hippocampus, Vol. 9, pp. 542-552.

Diamond teaches rats conditioned to exhibit recurrence of trauma upon repeated exposures to a cat (page 547, figure 1). As a patentable difference between the rat of Diamond and that of the claim cannot be discerned, the animal claimed is seen as the rat of Diamond produced by a different method. In the alternative, the rat of Diamond renders the claimed animal obvious as any differences would not affect the structure or use of the rat. Thus, Diamond anticipates or makes obvious the claimed invention.

Applicant argues model for PTSD disclosed is the only such model that resembles human PTSD. Applicant argues humans can exhibit PTSD years following an initial trauma. Applicant argues this process is "memorizing," and about 20% of the individuals exposed to a traumatic event will develop PTSD following re-exposure to a traumatic-like event. Applicant argues the method of traumatizing rats in the specification leads to animals suffering from chronic stress. Applicant argues Diamond exposed rats to the same trauma, and not a trauma-like event. Applicant argues each re-exposure occurred a short time after the previous exposure. Applicant argues Diamond's rats suffer from acute trauma, not chronic trauma as the claimed animals. Applicant states the inventor has evidence animals suffering from acute trauma and chronic trauma differentially regulate levels of DHEA. These arguments are not persuasive.

While it is understood that applicant's disclosed method produces a subpopulation of rats that exhibit PTSD symptoms, the rats of Diamond exhibit symptoms that fall within the scope of the claims. The presently disclosed method may be producing rats exhibiting chronic trauma, and thus are PTSD-like, but the rats of Diamond also exhibit the same symptoms. Further, the rats of Diamond are a product, and thus since they are taught by Diamond to re-experience trauma in response to a stimulus, and to exhibit hyper arousal in response to a stimulus, the ordinary artisan reasonably would have expected the rats of Diamond to avoid social contact. The non-observance of a phenotype associated with a product in the prior art does not make use of the prior art improper. With regards to DHEA levels, it is noted above Diamond

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teaches altered corticosterone levels in rats exposed to cats. Since DHEA is reported to stimulate corticosterone release, any evidence supplied by applicant would need to address the increased corticosterone levels in rats exposed to rats. Likewise, Wolframin and Sigma 1 receptor levels would be inherent. Applicant has provided no evidence that there is a structural alteration between the rats of Diamond and rats encompassed by the claims. There is no evidence that a discernable difference exists between acute trauma and chronic trauma so that one trauma can be distinguished from the other trauma. This is not to say there is no difference, just no difference is apparent on this record. To be persuasive, data must be submitted in the form of a declaration under 37 § CFR 1,132. At this point, there is no clear evidence that the rats of Diamond and those claimed do not exhibit the same symptoms and/or phenotypes.

Claims 6 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Diamond et al. (1999) Hippocampus, Vol. 9, pp. 542-552 in view of Cohen et al. (2000) Europ. Neuropsychopharmacology, Vol. 10, pp. 429-435.

Diamond teaches a method of producing rats affected by traumatic stress by determining the baseline level for 12 rats prior to exposure to a stressor, a cat (page 545, col. 1, parag. 2, lines 1-10). After exposure to the cat, the rats are retested in the six-arm maze (page 545, col. 1, parag. 2, lines 16-19 and page 547, col. 2, parag. 3, lines 1-7). Error rates were measured as the mean average of the group of rats testes (page 547, col. 2, parag. 3, lines 1-3).

Cohen teaches stress hormones, such as ATCH and corticosterone, alter after experiencing chronic stress, although the results seem to vary (page 433, col. 1, parag. 1, lines 1-10). Cohen also teaches in PTSD patients the conventional thought is cortisol is reduced (page 433, col. 1, parag. 1, lines 11-16). Cohen also teaches rats exposed to cat scent once, produced the generalized anxiety seen in PTSD patients (page 433, col. 1, parag. 2). Therefore Cohen offers teachings, suggestions and motivation to determine plasma levels of ATCH, corticosterone and cortisol in rats exhibiting PTSD behavior.

At the time of the instant invention, it would have been obvious to the ordinary artisan to produce rats exhibiting a PTSD behavior as taught by Diamond and further determining the effect of traumatic stress on plasma levels of ATCH, corticosterone and cortisol.

Applicant argues Cohen exposes rats to cat scent only once, and as such does not create PTSD rats. Applicant argues for reasons presented earlier in their response, Diamond also did not teach PTSD rats. Thus applicant argues the art cannot be combined. These arguments are not persuasive.

As rebutted above, Diamond teaches rats having two of the same phenotypes as in the animals of the claims, and that such conditioned rats have altered corticosterone levels. Thus, there is every reason for the art to monitor Diamond's physiologically as well as behaviorally.

Claims 6, 10 and 11 rejected under 35 U.S.C. 103(a) as being unpatentable over Diamond et al. (1999) Hippocampus, Vol. 9, pp. 542-552 in view of Adamec et al. (1999) Physiology and Behav., Vol. 65, pp. 723-737.

Diamond produced the rats by determining the baseline level for 12 rats prior to exposure to a stressor, a cat (page 545, col. 1, parag. 2, lines 1-10). After exposure to the cat, the rats are retested in the six-arm maze (page 545, col. 1, parag. 2, lines 16-19 and page 547, col. 2, parag. 3, lines 1-7). Error rates were measured as the mean average of the group of rats tested (page 547, col. 2, parag. 3, lines 1-3).

Adamec teaches determining passive behavior in cat-exposed rats by analyzing videotapes of rat-cat interactions for freezing (page 725, col. 1, parag. 5 and 6).

Therefore it would have been obvious to the ordinary artisan at the time of the instant invention to produced rats as taught by Diamond and analyze them for freezing as taught by Adamec.

Applicant argues the rats of Adamec exposed rats to cat scent once and thus the rats are suffering from acute trauma. Applicant argues the freezing observed in these rats was a passive defense and no anxiety as shown by the failure of anxiolytic drugs to affect freezing. Applicant argues since Diamond's rats did not suffer from PTSD, there would be no motivation to combine with Adamec. These arguments are not persuasive.

As stated early in this rebuttal, the rats of Diamond have 2 of the three claimed symptoms. Diamond is silent regarding the third symptom. However, Diamond notes an alteration in corticosterone levels in rats exposed to a cat. Thus, Diamond's rats are



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suffering from more than acute trauma. Adamec sets for the motivation to measure freezing, as did Cohen for physiological parameters.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah Crouch, Ph.D. whose telephone number is (571)272-0727. The examiner can normally be reached on M-Fri, 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Deborah Crouch/  
Primary Examiner, Art Unit 1632

January 15, 2009